08/656811 search 2

SYSTEM:OS - DIALOG OneSearch
File 154:MEDLINE(R) 1985-1997/Dec W3
(c) format only 1997 Knight-Ridder Info
File 155:MEDLINE(R) 1966-1997/Dec W3
(c) format only 1997 Knight-Ridder Info

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   Set Items Description
   --- ----- -----------
?s aplysia or drosophilia
        4186 APLYSIA
          72 DROSOPHILIA
   S1   4256 APLYSIA OR DROSOPHILIA
?s memory or facilitation
       72564 MEMORY
       13706 FACILITATION
   S2  85380 MEMORY OR FACILITATION
?s model
   S3 461974 MODEL
?s s1 adn s2 and s3
>>>Term "ADN" in invalid position
?s s1 and s2 and s3
        4256 S1
       85380 S2
      461974 S3
   S4     57 S1 AND S2 AND S3
?rd
...examined 50 records (50)
...completed examining records
   S5     32 RD (unique items)
?t s5/3,ab,kwic/1-32
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5/3,AB,KWIC/1 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09267022 97442493
Modulation of a cAMP/protein kinase A cascade by protein kinase C in sensory neurons of *Aplysia*.
Sugita S; Baxter DA; Byrne JH
Department of Neurobiology and Anatomy, The University of Texas Medical
School at Houston, Houston, Texas 77225, USA.
J Neurosci (UNITED STATES) Oct 1 1997, 17 (19) p7237-44, ISSN 0270-6474 Journal Code: JDF
Contract/Grant No.: K05 MH-00649, MH, NIMH; R01 NS-19895, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The synaptic connections between the sensory neurons of *Aplysia* and their follower neurons have been used as a *model* system for examining the cellular mechanisms contributing to neuronal and synaptic plasticity. Recent studies suggest that at least two protein kinases, protein kinase A (PKA) and protein kinase C (PKC), contribute to serotonin (5-HT)-induced short-term *facilitation*. The interaction between these two kinase cascades has not been examined, however. Using electrophysiological and biochemical approaches, we examined possible interactions between PKA and PKC cascades. The results indicated that prolonged activation of PKC by preincubation with phorbol esters attenuated PKA-mediated actions of 5-HT, including increases in sensory neuron excitability and spike broadening in the presence of tetraethylammonium (TEA) and nifedipine. Although phorbol esters also attenuated increases in excitability by an analog of cAMP and small cardioactive peptide B (SCPB), the degree of attenuation was smaller. In addition, phorbol esters did not attenuate broadening of TEA spikes by the cAMP analog and SCPB. Thus, phorbol esters appeared specifically to attenuate aspects of the 5-HT activation of the cAMP/PKA cascade. Measurements of cAMP levels with radioimmunoassays revealed that phorbol
esters did not attenuate 5-HT-induced cAMP synthesis, however. Finally, the results indicated that phorbol esters themselves induced a small but significant increase in excitability as well as an increase in the level of cAMP. Our results suggest that there is crosstalk between the PKC and PKA cascades. The mechanisms by which phorbol esters specifically attenuate 5-HT-induced activation of the cAMP/PKA cascade are not known, however.

Modulation of a cAMP/protein kinase A cascade by protein kinase C in sensory neurons of *Aplysia*.
The synaptic connections between the sensory neurons of *Aplysia* and their follower neurons have been used as a *model* system for examining the cellular mechanisms contributing to neuronal and synaptic plasticity. Recent studies suggest that at least two protein kinases, protein kinase A (PKA) and protein kinase C (PKC), contribute to serotonin (5-HT)-induced short-term *facilitation*. The interaction between these two kinase cascades has not been examined, however. Using electrophysiological and biochemical approaches, we examined possible interactions between PKA and PKC...
; Action Potentials--Drug Effects--DE; *Aplysia*--Physiology--PH; Cyclic AMP--Pharmacology--PD; Enzyme Activation; Neurons, Afferent--Drug Effects
--DE; Neuropeptides--Pharmacology--PD; Phorbol Esters--Pharmacology--PD;
Protein Kinase C--Metabolism--ME...

5/3,AB,KWIC/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09120201 97238274
Realistic simulation of the *Aplysia* siphon-withdrawal reflex circuit: roles of circuit elements in producing motor output. ✓
Lieb JR Jr; Frost WN
Department of Neurobiology and Anatomy, University of Texas, Houston Health Science Center 77225, USA.
J Neurophysiol (UNITED STATES) Mar 1997, 77 (3) p1249-68, ISSN
0022-3077 Journal Code: JC7
Contract/Grant No.: MH-10471, MH, NIMH; MH-48536, MH, NIMH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The circuitry underlying the *Aplysia* siphon-elicited siphon-withdrawal reflex has been widely used to study the cellular substrates of simple forms of learning and *memory*. Nonetheless, the functional roles of the different neurons and synaptic connections modified with learning have yet to be firmly established. In this study we constructed a realistic computer simulation of the best-understood component of this network to better understand how the siphon-withdrawal circuit works. We used an integrate-and-fire scheme to simulate four neuron types (LFS, L29, L30, L34) and 10 synaptic connections. Each of these circuit components was individually constructed to match the mean or typical example of its biological counterpart on the basis of group measurements of each circuit element. Once each cell and synapse was modeled, its free parameters were fixed and not subject to further manipulation. The LFS motor neurons respond to sensory input with a brief phasic burst followed by a long-lasting period of tonic firing. We found that the assembled *model* network responded to sensory input in a qualitatively similar fashion, suggesting that many of the interneurons important for producing the LFS firing response have now been identified. By selectively removing different circuit elements, we determined the contribution of each of the LFS firing pattern. Our first finding was that the monosynaptic sensory neuron to motor neuron pathway contributed only to the initial brief burst of the LFS firing response, whereas the polysynaptic pathway determined the overall duration of LFS firing. By making more selective deletions, we found that the circuit elements responsible for transforming brief sensory neuron discharges into long-lasting LFS firing were the slow components of the L29-LFS fast/slow excitatory postsynaptic potentials. The inhibitory L30 neurons exerted a significant braking action on the flow of excitatory information through the circuit. Interestingly, L30 lost its ability to reduce the duration of LFS firing at high stimulus intensities. This was found to be due to the intrinsic nature of L30's current-frequency relationship. Some circuit elements, including interneuron L34, and the electrical coupling between L29 and L30 were found to have little impact when subtracted from the network. These results represent a detailed dissection of the functional roles of the different elements of the siphon-elicited siphon-withdrawal circuit in *Aplysia*. Because many vertebrate and invertebrate circuits perform similar tasks and contain similar information processing elements, aspects of these results may be of general significance for understanding the function of motor networks. In addition, because several sites in this network store learning-related information, these results are relevant to elucidating the functional significance of the distributed storage of learned information in *Aplysia*
.

Realistic simulation of the *Aplysia* siphon-withdrawal reflex circuit: roles of circuit elements in producing motor output.
The circuitry underlying the *Aplysia* siphon-elicited siphon-withdrawal reflex has been widely used to study the cellular substrates of simple forms of learning and *memory*. Nonetheless, the functional roles of the different neurons and synaptic connections modified with learning have yet

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... from the network. These results represent a detailed dissection of the functional roles of the different elements of the siphon-elicited siphon-withdrawal circuit in *Aplysia*. Because many vertebrate and invertebrate circuits perform similar tasks and contain similar information processing elements, aspects of these results may be of general significance for...

... sites in this network store learning-related information, these results are relevant to elucidating the functional significance of the distributed storage of learned information in *Aplysia*.

Descriptors: *Aplysia*--Physiology--PH; *Muscles--Physiology--PH; *Nerve Net--Physiology--PH; *Reflex--Physiology--PH

5/3,AB,KWIC/3 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09070098 97205705

Neurobiological principles of learning and *memory*.

Brunelli M; Garcia-Gil M; Mozzachiodi R; Scuri R; Zaccardi ML

Dipartimento di Fisiologia e Biochimica G. Moruzzi, Universita degli Studi di Pisa, Italia.

Arch Ital Biol (ITALY) Jan 1997, 135 (1) p15-36, ISSN 0003-9829 Journal Code: 7I8

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

An increasing flow of evidences collected on elementary forms of learning processes in selected animal models evidentiates some mechanisms which can represent the basic cellular principles underlying plastic changes: 1. 5HT and second messengers of nucleotide type (like cAMP) have a pivotal role in the learning process. 2. In almost all short-term learning processes the modifications are subserved by a mechanism of protein phosphorylation. 3. In various animal models the modulation of K+ and Ca2+ channels is the molecular mechanism for learning. Experiments performed in sensory T neuron of the leech indicate that the modulation of Na+/K+ electrogenic pump is one of the fundamental mechanism for learning. 4. In long-term plastic changes, the most important finding is that newly synthesized proteins are formed. 5. In addition to what has been observed in the *Aplysia* *model*, where changes in synaptic efficacy represent the basic principles of *memory* storage, in the leech it has been demonstrated that a molecular machinery present in a single neuron can adapt the activity of the cell to environmental stimuli.

Neurobiological principles of learning and *memory*.

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Descriptors: Brain--Physiology--PH; *Learning--Physiology--PH; **Memory*
--Physiology--PH; Amnesia; *Aplysia*; Brain--Metabolism--ME; Calcium Channels--Physiology--PH; Leeches; Models, Neurological; Models, Psychological; Na(+)-K(+)-Exchanging ATPase--Metabolism--ME; Neurobiology
--Methods--MT; Neurons--Physiology--PH; Potassium...

5/3,AB,KWIC/4 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09049574 97171314

Differential effects of 4-aminopyridine, serotonin, and phorbol esters on *facilitation* of sensorimotor connections in *Aplysia*.

Sugita S; Baxter DA; Byrne JH

Department of Neurobiology and Anatomy, University of Texas Medical School-Houston 77225, USA.

J Neurophysiol (UNITED STATES) Jan 1997, 77 (1) p177-85, ISSN 0022-3077 Journal Code: JC7

Contract/Grant No.: K05MH-00649, MH, NIMH; R01NS-19895, NS, NINDS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Serotonergic modulation of sensory neurons in *Aplysia* and their synaptic connections with follower cells has been used extensively as a *model* system with which to study mechanisms underlying neuronal plasticity. Serotonin (5-HT)-induced *facilitation* of sensorimotor connections is due to at least two processes: a process related to the broadening of presynaptic action potentials and a spike-duration-independent (SDI) process that may involve mobilization of transmitter. We have examined the relationship between spike broadening and synaptic *facilitation* of relatively nondepressed sensorimotor connections in the intact pleural-pedal ganglia. Previously, 5-HT-induced spike broadening in the sensory neuron was shown to be primarily due to the modulation of a voltage-dependent K+ current (Ik.v). Low concentrations (20-30 microM) of 4-aminopyridine (4-AP) were used to rather selectively block Ik.v. 4-AP increased spike duration in the sensory neuron and the excitatory postsynaptic potential (EPSP) in the motor neuron. The temporal development of 4-AP-induced spike broadening closely parallel that of synaptic *facilitation*. Thus spike broadening via the reduction of Ik.v can directly contribute to synaptic *facilitation*. The relationship between spike broadening induced by 5-HT (10 microM) and enhancement of the
EPSP was also analyzed. We found that components of 5-HT-induced synaptic
facilitation preceded the development of 5-HT-induced spike broadening. The comparison between the results of 4-AP and 5-HT revealed that the SDI processes made an important contribution to the rapid development of 5-HT-induced synaptic *facilitation* and that spike broadening made an important contribution to its maintenance. The SDI process and a slowly developing component of 5-HT-induced spike broadening are mediated, at least in part, by the activation of protein kinase C (PKC). Application of phorbol 12,13-diacetate (PDAc), an activator of PKC, partially mimicked the effects of 5-HT on spike duration and the EPSP. PDAc-induced enhancement of
the EPSP preceded the slower development of PDAc-induced spike broadening.
Like 5-HT, PDAc enhanced the EPSP via both spike broadening and the SDI processes. In addition, a 15-min exposure to PDAc occluded 5-HT-induced enhancement of the EPSP, suggesting that PKC and 5-HT engage similar or overlapping mechanisms. On the basis of these results and others, we propose a time-dependent hypothesis for the 5-HT-induced synaptic *facilitation* of nondepressed synapses, in which multiple second-messenger/protein kinase systems mediate the actions of 5-HT via both spike-duration-dependent and SDI processes.

Differential effects of 4-aminopyridine, serotonin, and phorbol esters on *facilitation* of sensorimotor connections in *Aplysia*.

Serotonergic modulation of sensory neurons in *Aplysia* and their synaptic connections with follower cells has been used extensively as a *model* system with which to study mechanisms underlying neuronal plasticity. Serotonin (5-HT)-induced *facilitation* of sensorimotor connections is due to at least two processes: a process related to the broadening of presynaptic action potentials and a spike-duration-independent (SDI) process that may involve mobilization of transmitter. We have examined the relationship between spike broadening and synaptic *facilitation* of relatively nondepressed sensorimotor connections in the intact pleural-pedal ganglia. Previously, 5-HT-induced spike broadening in the sensory neuron was shown to be...

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second-messenger/protein kinase systems mediate the actions of 5-HT via both spike-duration-dependent and SDI processes.
Descriptors: *Aplysia*--Physiology--PH; *Intercellular Junctions--Drug Effects--DE; *Motor Neurons--Drug Effects--DE; *Neurons, Afferent--Drug Effects--DE; *Phorbol Esters--Pharmacology--PD;
*Serotonin--Pharmacology
--PD; *4...

5/3,AB,KWIC/5 (Item 5 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09009141 97153057
Spaced training induces normal long-term *memory* in CREB mutant mice.
Kogan JH; Frankland PW; Blendy JA; Coblentz J; Marowitz Z; Schutz G; Silva AJ
Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724, USA.
Curr Biol (ENGLAND) Jan 1 1997, 7 (1) p1-11, ISSN 0960-9822
Journal Code: B44
Contract/Grant No.: P01HD33098, HD, NICHD
Languages: ENGLISH
Document type: JOURNAL ARTICLE
BACKGROUND: The cAMP responsive element binding protein (CREB) is a
transcription factor the activity of which is modulated by increases in the intracellular levels of cAMP and calcium. Results from studies with *Aplysia*, Drosophila and mice indicate that CREB-activated transcription is required for long-term *memory*. Furthermore, a recent study found that long-term *memory* for olfactory conditioning can be induced with a single trial in transgenic Drosophila expressing a CREB activator, whereas in normal flies, with presumably lower CREB-mediated transcription levels, conditioning requires multiple spaced trials. This suggests that CREB-mediated transcription is important in determining the type of training required for long-term *memory* of olfactory conditioning in Drosophila. Interestingly, studies with cultured *Aplysia* neurons indicated that removing a CREB repressor promoted the formation of long-term *facilitation*, a cellular *model* of non-associative *memory*. RESULTS: Here, we have confirmed that mice lacking the alpha and Delta CREB
proteins (CREBalphaDelta-) have abnormal long-term, but not short-term, *memory*, as tested in an ethologically meaningful task. Importantly, additional spaced training can overcome the profound *memory* deficits of CREBalphaDelta- mutants. Increasing the intertrial interval from 1 to 60 minutes overcame the *memory* deficits of the CREBalphaDelta- mice in three
distinct behavioral tasks: contextual fear conditioning, spatial learning and socially transmitted food preferences. CONCLUSIONS: Previous findings
and results presented here demonstrate that CREB mutant mice have profound long-term *memory* deficits. Importantly, our findings indicate that manipulations of CREB function can affect the number of trials and the intertrial interval required for committing information to long-term *memory*. Remarkably, this effect of CREB function is not restricted to simple conditioning tasks, but also affects complex behaviours such as spatial *memory* and *memory* for socially transmitted food preferences.

Spaced training induces normal long-term *memory* in CREB mutant mice.
... CREB) is a transcription factor the activity of which is modulated by increases in the intracellular levels of cAMP and calcium. Results from studies with *Aplysia*, Drosophila and mice indicate that CREB-activated transcription is required for long-term *memory*. Furthermore, a recent study found that long-term *memory* for olfactory conditioning can be induced with a single trial in transgenic Drosophila expressing a CREB activator, whereas in normal flies, with presumably lower CREB...

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proteins (CREBalphaDelta-) have abnormal long-term, but not short-term, *memory*, as tested in an ethologically meaningful task. Importantly, additional spaced training can overcome the profound *memory* deficits of CREBalphaDelta- mutants. Increasing the intertrial interval from 1 to 60 minutes overcame the *memory* deficits of the CREBalphaDelta- mice in three
distinct behavioral tasks: contextual fear conditioning, spatial learning and socially transmitted food preferences. CONCLUSIONS: Previous findings
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Descriptors: DNA-Binding Protein, Cyclic AMP-Responsive--Genetics--GE; *
Memory--Physiology--PH

5/3,AB,KWIC/6 (Item 6 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08399619 95216138
The cellular basis of classical conditioning in *Aplysia* californica--it's less simple than you think.
Glanzman DL
Dept of Physiological Science, University of California, Los Angeles 90024 1568.
Trends Neurosci (ENGLAND) Jan 1995, 18 (1) p30-6, ISSN 0166-2236
Journal Code: WEL
Contract/Grant No.: NS29563, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Classical conditioning of the withdrawal reflex of the marine snail *Aplysia* californica can be used as an important *model* system for investigating the neurobiology of associative learning. It results when weak tactile stimulation of the snail's mantle shelf or siphon is repeatedly paired with strong electrical shocks to the animal's tail. This learned behavioral change is thought to be mediated by a presynaptic neuronal mechanism-activity-dependent presynaptic *facilitation* of the connections between sensory and motor neurons in the CNS of *Aplysia*. Recent evidence suggests, however, that another type of synaptic plasticity-Hebbian potentiation of the sensorimotor connections-might contribute to classical conditioning in *Aplysia*. Additional evidence indicates that this relatively simple form of learning is likely to be mediated by multiple neuronal mechanisms.

The cellular basis of classical conditioning in *Aplysia* californica--it's less simple than you think.
Classical conditioning of the withdrawal reflex of the marine snail *Aplysia* californica can be used as an important *model* system for investigating the neurobiology of associative learning. It results when weak tactile stimulation of the snail's mantle shelf or siphon is repeatedly paired...

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.; *Aplysia*; Models, Neurological; Neuronal Plasticity--Physiology--PH; Presynaptic Terminals--Physiology--PH; Psychomotor Performance--Physiology
--PH

5/3,AB,KWIC/7 (Item 7 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08365470 95395550
Structure of the network mediating siphon-elicited siphon withdrawal in *Aplysia*.
Frost WN; Kandel ER
Department of Neurobiology and Anatomy, University of Texas Medical School, Houston 77225, USA.
J Neurophysiol (UNITED STATES) Jun 1995, 73 (6) p2413-27, ISSN

0022-3077 Journal Code: JC7
Contract/Grant No.: MH-15174, MH, NIMH; MH-48536, MH, NIMH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
1. The network mediating siphon-elicited siphon withdrawal in *Aplysia* is a useful *model* system for cellular studies of simple forms of learning and *memory* . Here we describe three new cells in this circuit, L33, L34, and L35, and several new connections among the following network neurons: LE, L16, L29, L30, L32, L33, L34, and L35. On the basis of these findings we present an updated diagram of the network. Altogether, 100 neurons have now been identified in the abdominal ganglion that can participate in both siphon-elicited and spontaneous respiratory pumping siphon withdrawals. 2. Two features of the interneuronal population may have important behavioral functions. First, the L29 interneurons make fast and slow excitatory connections onto the LFS cells, which may be important for transforming brief sensory neuron discharges into the long-lasting motor neuron firing that underlies withdrawal duration. Second, inhibitory interneurons are prominent in the network. The specific connectivity of certain of these interneurons is appropriate to block potentially interfering inhibitory inputs from other networks during execution of the behavior. 3. Deliberate searches have so far revealed very few excitatory interneuronal inputs to the network interneurons and motor neurons within the abdominal ganglion. These results, together with intracellular studies by others, are more consistent at present with a relatively dedicated rather than a highly distributed organizational scheme for the siphon-elicited siphon withdrawal circuitry.

Structure of the network mediating siphon-elicited siphon withdrawal in *Aplysia*.
1. The network mediating siphon-elicited siphon withdrawal in *Aplysia* is a useful *model* system for cellular studies of simple forms of learning and *memory* . Here we describe three new cells in this circuit, L33, L34, and L35, and several new connections among the following network neurons: LE, L16, L29...
Descriptors: *Aplysia*--Physiology--PH; *Interneurons--Physiology--PH; *Nerve Net--Physiology--PH; Ganglia, Invertebrate; Learning; *Memory*; Motor Neurons--Physiology--PH

5/3,AB,KWIC/8 (Item 8 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08173273 95173669
Postsynaptic modifications in long-term *facilitation* in *Aplysia*: upregulation of excitatory amino acid receptors.
Trudeau LE; Castellucci VF
Laboratoire de neurobiologie et comportement, Institut de Recherches Cliniques de Montreal, Canada.
J Neurosci (UNITED STATES) Feb 1995, 15 (2) p1275-84, ISSN 0270-6474
Journal Code: JDF
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Long-term sensitization of the gill and siphon withdrawal in *Aplysia* is accompanied by *facilitation* of sensorimotor synaptic connections that depends on new protein synthesis. This phenomenon has been previously shown
to involve presynaptic growth. At the postsynaptic level, a reorganization should occur to parallel the formation of new synaptic contacts. We show here that 24 hr following an application of 5-HT, which produces long-term synaptic *facilitation* (LTF), the response of the motoneuron to an excitatory amino acid agonist of the synaptic receptors is increased. General inhibition of protein synthesis with anisomycin blocks this enhancement. Inhibiton of protein synthesis limited to the postsynaptic neuron by intracellular injection of gelonin, a ribosome-inactivating toxin, also blocks the increase in the response to the agonist but fails to block 24 hr LTF. These results are compatible with a *model* of LTF that involves coordinate pre- and postsynaptic changes. The latter may include an upregulation of functional postsynaptic receptors. These may not be initially required for LTF measured at a 24 hr time point, but could become necessary for later stages of LTF. An increase in the number of functional postsynaptic receptors in a reserve pool may also prime the postsynaptic neuron for subsequent learning-associated plasticity.

Postsynaptic modifications in long-term *facilitation* in *Aplysia*: upregulation of excitatory amino acid receptors.
Long-term sensitization of the gill and siphon withdrawal in *Aplysia* is accompanied by *facilitation* of sensorimotor synaptic connections that depends on new protein synthesis. This phenomenon has been previously shown
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... inactivating toxin, also blocks the increase in the response to the agonist but fails to block 24 hr LTF. These results are compatible with a *model* of LTF that involves coordinate pre- and postsynaptic changes. The latter may include an upregulation of functional postsynaptic receptors. These may not be initially required...
Descriptors: *Aplysia*--Physiology--PH; *Receptors, Amino Acid --Metabolism--ME; *Synapses--Physiology--PH; *Up-Regulation (Physiology)

5/3,AB,KWIC/9 (Item 9 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08061570 95041366
Memory. A *model* with good CREdentials.
Stevens CF; Verma I
Salk Institute, La Jolla, California 92037.
Curr Biol (ENGLAND) Aug 1 1994, 4 (8) p736-8, ISSN 0960-9822
Journal Code: B44
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The sea snail *Aplysia* provides a relatively simple *model* system for studying both short-term and long-term *memory*; a known transcriptional mechanism is implicated in establishment of the latter.

Memory. A *model* with good CREdentials.
The sea snail *Aplysia* provides a relatively simple *model* system for studying both short-term and long-term *memory*; a known transcriptional mechanism is implicated in establishment of the latter.
Descriptors: *Aplysia*--Physiology--PH; *Avoidance Learning--Physiology --PH; **Memory*--Physiology--PH; *Transcription, Genetic

5/3,AB,KWIC/10 (Item 10 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08033689 95007782
Deficient long-term *memory* in mice with a targeted mutation of the cAMP-responsive element-binding protein.
Bourtchuladze R; Frenguelli B; Blendy J; Cioffi D; Schutz G; Silva AJ
Cold Spring Harbor Laboratory, New York 11724.
Cell (UNITED STATES) Oct 7 1994, 79 (1) p59-68, ISSN 0092-8674
Journal Code: CQ4
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The cAMP-responsive element-binding protein (CREB) has been implicated in
the activation of protein synthesis required for long-term *facilitation*, a cellular *model* of *memory* in *Aplysia* . Our studies with fear conditioning and with the water maze show that mice with a targeted disruption of the alpha and delta isoforms of CREB are profoundly deficient in long-term *memory*. In contrast, short-term *memory*, lasting between 30 and 60 min, is normal. Consistent with models claiming a role for long-term potentiation (LTP) in *memory*, LTP in hippocampal slices from CREB mutants
decayed to baseline 90 min after tetanic stimulation. However, paired-pulse *facilitation* and posttetanic potentiation are normal. These results implicate CREB-dependent transcription in mammalian long-term *memory*.
Deficient long-term *memory* in mice with a targeted mutation of the cAMP-responsive element-binding protein.
The cAMP-responsive element-binding protein (CREB) has been implicated in
the activation of protein synthesis required for long-term *facilitation*, a cellular *model* of *memory* in *Aplysia* . Our studies with fear conditioning and with the water maze show that mice with a targeted disruption of the alpha and delta isoforms of CREB are profoundly deficient in long-term *memory*. In contrast, short-term *memory*, lasting between 30 and 60 min, is normal. Consistent with models claiming a role for long-term potentiation (LTP) in *memory*, LTP in hippocampal slices from CREB

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Descriptors: DNA-Binding Protein, Cyclic
AMP-Responsive--Physiology--PH;
**Memory*--Physiology--PH; *Mutation--Physiology--PH

5/3,AB,KWIC/11 (Item 11 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08015020 94375481
Differential phosphorylation of neuronal substrates by catalytic subunits of *Aplysia* cAMP-dependent protein kinase with alternative N termini.
Panchal RG; Cheley S; Bayley H
Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts 01545.
J Biol Chem (UNITED STATES) Sep 23 1994, 269 (38) p23722-30, ISSN
0021-9258 Journal Code: HIV
Contract/Grant No.: NS26760, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
cAMP-dependent protein kinase (PKA) is an important participant in neuronal modulation: the ability of neurons to change their properties in response to external stimuli. In *Aplysia* mechanosensory neurons, PKA plays roles in both short and long term presynaptic *facilitation*, which is a simple *model* for learning and *memory*. PKA in *Aplysia* is a collection of structurally and functionally diverse regulatory and catalytic (C) subunits. We have argued that this diversity may in part account for the ability of the enzyme to take part in neuronal events that are spatially and temporally separated. Here, we add credence to this hypothesis by showing that C subunits of *Aplysia* PKA with alternative N termini target different substrates in subcellular fractions from *Aplysia* neurons, despite their similar actions on synthetic peptide substrates. Purified recombinant CAPL-AN1A1, which has an N terminus that is homologous
to the myristylated sequence described in mammals, catalyzes the formation of two phosphoproteins of 24 and 8 kDa more rapidly than CAPL-AN2A1, which
has a distinct N terminus weakly related to that of the yeast TPK1 gene product. The 24-kDa phospoprotein, but not the 8-kDa species, is detected in taxol-stabilized microtubules, suggesting that it is associated with the cytoskeleton. CAPL-AN2A1, in contrast, generates a 55-kDa phosphoprotein that is not observed with CAPL-AN1A1. The 55-kDa species is found in the detergent supernatant of the cytoskeleton fraction. Differential targeting of substrates by C subunits of PKA may therefore contribute to the ability of this kinase to play multiple roles in neuronal modulation.

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sequence...
Descriptors: *Aplysia*--Enzymology--EN; *Cyclic AMP-Dependent Protein
Kinases--Metabolism--ME; *Nerve Tissue Proteins--Metabolism--ME

5/3,AB,KWIC/12 (Item 12 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07798066 93348233
L-glutamate may be the fast excitatory transmitter of *Aplysia* sensory neurons.
Dale N; Kandel ER
Center for Neurobiology and Behavior, Columbia University, College of Physicians and Surgeons, New York, NY 10032.
Proc Natl Acad Sci U S A (UNITED STATES) Aug 1 1993, 90 (15) p7163-7,
ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Although modulation of synaptic transmission between *Aplysia* mechanosensory and motor neurons has been an important *model* for processes thought to underlie simple forms of learning and *memory*, the nature of the fast excitatory transmitter utilized by the sensory neurons has remained obscure. To identify the sensory neuron transmitter, we first examined the detailed properties of the synaptic response evoked in motor neurons cocultured with pleural sensory neurons. The excitatory postsynaptic current had a nonlinear current-voltage relation with a reversal potential between 0 and 10 mV and a plateau region between -40 and -70 mV. When the concentration of Mg2+ in the artificial sea water was lowered to 5 mM, the current-voltage relation of the excitatory postsynaptic current became linear, suggesting that Mg2+ blocks the postsynaptic receptor in a voltage-dependent manner. After screening a variety of small molecules, we found that L-glutamate could mimic the actions of the sensory neuron transmitter: responses to L-glutamate also had a reversal potential between 0 and 10 mV and a nonlinear current-voltage relation that could be made linear by lowering external Mg2+. To demonstrate further similarity of action between L-glutamate and the endogenous transmitter, we utilized four antagonists (kynurenate, 6,7-dinitroquinoxaline-2,3-dione, D-aspartate, and D-glutamate) to block in a dose-dependent manner the actions of L-glutamate and the natural transmitter. We therefore suggest that the sensory neurons use a glutamate-like transmitter and favor L-glutamate itself, because no other naturally occurring amino acid that we have studied has had similar actions. As the postsynaptic receptor for the sensory neuron transmitter is weakly blocked in a voltage-dependent manner by Mg2+, the excitatory receptors innervated by the *Aplysia* sensory neuron may represent a distant precursor of the vertebrate N-methyl-D-aspartate receptor.

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Descriptors: *Aplysia*--Physiology--PH; *Glutamates--Physiology--PH; *Neurons, Afferent--Physiology--PH; *Neurotransmitters--Physiology--PH

5/3,AB,KWIC/13 (Item 13 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07742598 94125144
The role of interneurons in controlling the tail-withdrawal reflex in *Aplysia*: a network *model*.
White JA; Ziv I; Cleary LJ; Baxter DA; Byrne JH
Department of Neurobiology and Anatomy, University of Texas Medical School, Houston 77225.
J Neurophysiol (UNITED STATES) Nov 1993, 70 (5) p1777-86, ISSN
0022-3077 Journal Code: JC7
Contract/Grant No.: MH-10215, MH, NIMH; MH-00649, MH, NIMH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
1. The contributions of monosynaptic and polysynaptic circuitry to the tail-withdrawal reflex in the marine mollusk *Aplysia* californica were assessed by the use of physiologically based neural network models. Effects of monosynaptic circuitry were examined by the use of a two-layer network *model* with four sensory neurons in the input layer and one motor neuron in the output layer. Results of these simulations indicated that the monosynaptic circuit could not account fully for long-duration responses of

tail motor neurons elicited by tail stimulation. 2. A three-layer network *model* was constructed by interposing a layer of two excitatory interneurons between the input and output layers of the two-layer network *model* . These interneurons had properties mimicking those of the recently described interneuron LP117, receiving excitatory input from pleural sensory neurons and evoking a biphasic excitatory postsynaptic potential (EPSP) in pedal motor neurons (Cleary and Byrne 1993). The three-layer *model* could account for long-duration responses in motor neurons. 3. Sensory neurons are a known site of plasticity in *Aplysia*. Synaptic plasticity was incorporated into the three-layer *model* by altering the magnitudes of conductance changes evoked in motor neurons and interneurons by presynaptic sensory neurons. In these simulations the excitatory interneurons converted an amplitude-coded input into an amplitude- and duration-coded output, allowing the three-layer network to support a large range of output amplitudes and durations. 4. Synaptic plasticity at more than one locus modified dramatically the input-output relationship of the three-layer network *model*. This feature gave the *model* redundancy in its plastic properties and points to the possibility of distributed *memory* in the circuitry mediating withdrawal reflexes in *Aplysia*. Multiple sites of control over the response of the network would likely allow a more diverse repertoire of responses.

The role of interneurons in controlling the tail-withdrawal reflex in *Aplysia*: a network *model*.

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; *Aplysia*; Membrane Potentials--Physiology--PH; Motor Neurons --Physiology--PH; Neuronal Plasticity--Physiology--PH; Receptors, Sensory --Physiology--PH; Tail--Innervation--IR

5/3,AB,KWIC/14 (Item 14 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07532351 93240233
Functional uncoupling of inhibitory interneurons plays an important role in short-term sensitization of *Aplysia* gill and siphon withdrawal reflex.
Trudeau LE; Castellucci VF
Laboratoire de Neurobiologie et Comportement, Institut de recherches cliniques de Montreal, Quebec, Canada.
J Neurosci (UNITED STATES) May 1993, 13 (5) p2126-35, ISSN 0270-6474
Journal Code: JDF
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Attempts to explain learning-associated potentiation of synaptic transmission in *model* systems such as withdrawal reflexes in the mollusk *Aplysia* or the hippocampus of vertebrates have focused on the mechanisms by which transmitter release is increased in the principal elements of the circuit. Increased transmission in neuronal networks such as the gill and siphon withdrawal reflex (GSWR) of *Aplysia* may, however, also be caused by a decrease of transmitter release by inhibitory interneurons. The importance and function of cholinergic inhibitory transmission in the GSWR network were investigated. Central application of the nicotinic cholinergic antagonist d-tubocurarine (d-TC) considerably potentiated gill contractions, evoked either by nerve stimulation or by tactile stimulation of the siphon. Compound EPSPs evoked in motoneurons upon siphon nerve stimulation were also significantly prolonged following application of d-TC, but were unaffected by hexamethonium, a blocker of excitatory ACh receptors in *Aplysia*. Recordings from excitatory interneurons showed that they received excitation followed by powerful inhibitory input upon stimulation of the siphon nerve. Application of d-TC completely blocked this rapid inhibition, thus prolonging the compound EPSPs evoked in the interneurons. These effects were obtained at a concentration of d-TC (100 microM) that almost totally blocked fast inhibitory cholinergic transmission, but was without effect on monosynaptic connections between sensory neurons and motoneurons of the reflex. *Facilitation* of (1) compound EPSCs in motoneurons and (2) evoked excitatory interneuronal firing was reduced in preparations already disinhibited by pretreatment with d-TC. *Facilitation* of sensory-motor synapses, however, was not reduced in the presence of d-TC, indicating that facilitatory interneurons are still activated under cholinergic blockade. These data show that transmission through the GSWR neuronal network is gated by a feedback inhibitory mechanism. They also suggest that a reduction of cholinergic inhibition onto excitatory interneurons may be a mechanism through which transmission within the GSWR network is increased during various forms of learning, such as sensitization. These data place new emphasis on the important role of inhibitory interneurons in determining the plastic properties of neuronal networks, in both invertebrates and vertebrates.

Functional uncoupling of inhibitory interneurons plays an important role in short-term sensitization of *Aplysia* gill and siphon withdrawal reflex.
Attempts to explain learning-associated potentiation of synaptic transmission in *model* systems such as withdrawal reflexes in the mollusk *Aplysia* or the hippocampus of vertebrates have focused on the mechanisms by which transmitter release is increased in the principal elements of the circuit. Increased transmission in neuronal networks such as the gill and siphon withdrawal reflex (GSWR) of *Aplysia* may, however, also be caused by a decrease of transmitter release by inhibitory interneurons. The importance and function of cholinergic inhibitory transmission in the GSWR ...

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Descriptors: *Aplysia*--Physiology--PH; *Gills--Physiology--PH; *Interneu rons--Physiology--PH; *Neural Inhibition; *Reflex--Physiology--PH

5/3,AB,KWIC/15 (Item 15 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07464605 92407607
Involvement of protein kinase C in serotonin-induced spike broadening and synaptic *facilitation* in sensorimotor connections of *Aplysia*.
Sugita S; Goldsmith JR; Baxter DA; Byrne JH
Department of Neurobiology and Anatomy, University of Texas Medical School, Houston 77225.
J Neurophysiol (UNITED STATES) Aug 1992, 68 (2) p643-51, ISSN 0022-3077 Journal Code: JC7
Contract/Grant No.: MH-00649, MH, NIMH; RO1-NS-19895, NS, NINDS;
T32-HD-07324, HD, NICHD
Languages: ENGLISH
Document type: JOURNAL ARTICLE
1. Plasticity at the connections between sensory neurons and their follower cells in *Aplysia* has been used extensively as a *model* system to examine mechanisms of simple forms of learning. Earlier studies have

concluded that serotonin (5-HT) is a key modulatory transmitter and that it exerts its short-term actions via cAMP-dependent activation of protein kinase A. Subsequently, it has become clear that other kinase systems such as protein kinase C (PKC) also may be involved in the actions of 5-HT. 2. Application of phorbol esters, which activate PKC, produced a slowly developing spike broadening but had little effect on excitability (a process known to be primarily cAMP dependent). Moreover, the effects of phorbol esters and 5-HT on spike duration were not additive, suggesting that they may share some common mechanisms. 3. The protein kinase inhibitor staurosporine suppressed both 5-HT-induced slowly developing spike broadening and, under certain conditions, *facilitation* of transmitter release. Staurosporine did not inhibit 5-HT-induced enhancement of excitability. The effectiveness of staurosporine on spike broadening was dependent on the time at which spike broadening was examined after application of 5-HT. Staurosporine appeared to have little effect on spike broadening 3 min after application of 5-HT, whereas it inhibited significantly 5-HT-induced spike broadening at later times. The staurosporine-insensitive component of 5-HT-induced spike broadening may be mediated by cAMP. 4. The results suggest that the activation of PKC plays a key role in components of both 5-HT-induced spike broadening and *facilitation* of synaptic transmission.(ABSTRACT TRUNCATED AT 250 WORDS)

Involvement of protein kinase C in serotonin-induced spike broadening and synaptic *facilitation* in sensorimotor connections of *Aplysia*.
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Descriptors: *Aplysia*--Physiology--PH; *Evoked Potentials, Somatosensory --Drug Effects--DE; *Protein Kinase C--Physiology--PH; *Serotonin --Pharmacology--PD; *Somatosensory Cortex--Physiology--PH; *Synapses--Drug
Effects--DE

5/3,AB,KWIC/16 (Item 16 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07403314 93164449
[Synaptic plasticity and gene products]
Sekino Y; Kuroda Y
Dept. of Molecular and Cellular Neurobiology, Tokyo Metropolitan Institute for Neurosciences.
Nippon Rinsho (JAPAN) Nov 1992, 50 (11) p2796-807, ISSN 0047-1852
Journal Code: KIM
Languages: JAPANESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English
Abstract
Synaptic plasticity is thought to be the basic mechanism underlying learning and *memory*. The cellular mechanisms underlying synaptic plasticity have been extensively investigated in invertebrates and in vertebrates. What is the nature of synaptic plasticity? Can genes and gene products regulate plasticity? If so, how? The behavioral sensitization of the gill-and-siphon-withdrawal reflex of *Aplysia* is a simple *model* of plasticity in invertebrates, and can be examined in dissociated cell culture. Using a *model* of plasticity in cell culture, the molecular cascades of both short-term and long-term sensitization have been investigated, and characterized. Both gene transcription and protein synthesis were shown to contribute to the long-term sensitization. Long-term potentiation (LTP) is a well-characterized *model* for synaptic plasticity in vertebrates. Many possible cascades have been proposed, but it has not yet been settled whether an increase of transmitter release from presynaptic terminal, an increase of synaptic current, is responsible for the maintenance of LTP. Inhibition of protein synthesis resulted in a failure to maintain LTP over 3-4 hours. Thus, new protein synthesis may be needed for the maintenance of LTP. Induction of so-called immediate early genes that are induced immediately upon depolarization or neurotransmitter stimulation of the neuron has been studied as a possible mechanism underlying LTP. However, there is no good evidence yet implicating gene regulation to be involved in plasticity in vertebrates.

Synaptic plasticity is thought to be the basic mechanism underlying learning and *memory*. The cellular mechanisms underlying synaptic plasticity have been extensively investigated in invertebrates and in vertebrates. What is the nature of synaptic plasticity? Can genes and gene products regulate plasticity? If so, how? The behavioral sensitization of the gill-and-siphon-withdrawal reflex of *Aplysia* is a simple *model* of plasticity in invertebrates, and can be examined in dissociated cell culture. Using a *model* of plasticity in cell culture, the molecular cascades of both short-term and long-term sensitization have been investigated, and characterized. Both gene transcription and protein synthesis were shown to contribute to the long-term sensitization. Long-term potentiation (LTP) is a well-characterized *model* for synaptic plasticity in vertebrates. Many possible cascades have been proposed, but it has not yet been settled whether an increase of transmitter release from
...
; Action Potentials; *Aplysia*; Gene Expression; Hippocampus--Physiology --PH; Learning; *Memory*; Neurotransmitters--Metabolism--ME; Synapses
--Metabolism--ME

5/3,AB,KWIC/17 (Item 17 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07204977 92385619
An analytical short- and long-term *memory* *model* of presynaptic plasticity.
Ciaccia P; Maio D; Vacca GP
Dipartimento di Elettronica, Informatica e Sistemistica, Universita di Bologna-CIOC-CNR, Italy.
Biol Cybern (GERMANY) 1992, 67 (4) p335-45, ISSN 0340-1200
Journal Code: A2H
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A mathematical *model*, called the Learning Gate *Model* (LGM), that describes phenomena responsible for biological synaptic plasticity, is presented. The functionality of the *model* are mainly based on the work of Kandel and colleagues on the most elementary forms of learning observed in the *Aplysia* Californica marine mollusc. In particular, emphasis is placed on the double temporal dynamics of synaptic plasticity and the temporal specificity of classical conditioning. By properly modeling the effect of the binding of Ca++ ions to the serotonin-sensitive adenylate cyclase enzyme, it is shown how a positively accelerated learning curve can be obtained for sensitization and classical conditioning. Phenomena of spontaneous recovery and second-order conditioning are reproduced through simulations. Mathematical analyses of the temporal trace of conditioned stimulus and of the Short-Term *Memory* steady state are also given.

An analytical short- and long-term *memory* *model* of presynaptic plasticity.
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Descriptors: *Memory*--Physiology--PH; *Models, Neurological; *Neuronal
Plasticity--Physiology--PH; Conditioning, Classical; Mathematics; *Memory*, Short-Term--Physiology--PH

5/3,AB,KWIC/18 (Item 18 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07019780 91353940
Neural and molecular bases of nonassociative and associative learning in *Aplysia*.
Byrne JH; Baxter DA; Buonomano DV; Cleary LJ; Eskin A; Goldsmith JR;
McClendon E; Nazif FA; Noel F; Scholz KP
Department of Neurobiology and Anatomy, University of Texas Medical School, Houston 77225.
Ann N Y Acad Sci (UNITED STATES) 1991, 627 p124-49, ISSN 0077-8923
Journal Code: 5NM
Contract/Grant No.: F31 MH09895, MH, NIMH; F31 MH09956, MH, NIMH; T32
HD07324, HD, NICHD; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
A *model* that summarizes some of the neural and molecular mechanisms contributing to short- and long-term sensitization is shown in Figure 14. Sensitizing stimuli lead to the release of a modulatory transmitter such as 5-HT. Both serotonin and sensitizing stimuli lead to an increase in the synthesis of cAMP and the modulation of a number of K+ currents through protein phosphorylation. Closure of these K+ channels leads to membrane depolarization and the enhancement of excitability. An additional consequence of the modulation of the K+ currents is a reduction of current during the repolarization of the action potential, which leads to an increase in its duration. As a result, Ca2+ flows into the cell for a correspondingly longer period of time, and additional transmitter is released from the cell. Modulation of the pool of transmitter available for release (mobilization) also appears to occur as a result of sensitizing stimuli. Recent evidence indicates that the mobilization process can be activated by both cAMP-dependent protein kinase and protein kinase C. Thus, release of transmitter is enhanced not only because of the greater influx of Ca2+ but also because more transmitter is made available for release by mobilization. The enhanced release of transmitter leads to enhanced activation of motor neurons and an enhanced behavioral response. Just as the regulation of membrane currents is used as a read out of the *memory* for short-term sensitization, it also is used as a read out of the *memory* for long-term sensitization. But long-term sensitization differs from short-term sensitization in that morphological changes are associated with it, and long-term sensitization requires new protein synthesis. The mechanisms that induce and maintain the long-term changes are not yet fully understood (see the dashed lines in Fig. 14) although they are likely to be due to direct interactions with the translation apparatus and perhaps also to events occurring in the cell nucleus. Nevertheless, it appears that the same intracellular messenger, cAMP, that contributes to the expression of the short-term changes, also triggers cellular processes that lead to the long-term changes. One possible mechanism for the action of cAMP is through its regulation of the synthesis of membrane modulatory proteins or key effector proteins (for example, membrane channels). It is also possible that long-term changes in membrane currents could be due in part to enhanced activity of the cAMP-dependent protein kinase so that there is a persistent phosphorylation of target proteins.(ABSTRACT TRUNCATED AT 400
WORDS)

Neural and molecular bases of nonassociative and associative learning in *Aplysia*.
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Descriptors: *Aplysia*--Physiology--PH; *Association Learning--Physiology--PH; *Brain--Physiology--PH; *Learning--Physiology--PH

5/3,AB,KWIC/19 (Item 19 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

06176086 85147634
Cellular mechanisms of learning, *memory*, and information storage.
Farley J; Alkon DL
Annu Rev Psychol (UNITED STATES) 1985, 36 p419-94, ISSN 0066-4308
Journal Code: 6EB
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW
In Table 1, we summarize what is convincingly demonstrated to date for the major vertebrate and invertebrate *model* systems attempting to elucidate cellular mechanisms of associative learning. Two major concerns are the adequacy of the behavioral demonstrations and the completeness and extent of the accompanying neurophysiology. In addressing the issue of behavior, it is important to define clearly which criteria are both necessary and sufficient to infer the involvement of an associative-learning process. Similarly, it is also important to distinguish among those primary characteristics of associative learning in general, and those secondary or tertiary features that serve to define various subclasses. In our view, it would be unreasonable to require that any given preparation exhibit all the defining features of classical conditioning, for example, in order to qualify as a "legitimate" instance of associative learning. This is especially true if the goal is to understand the more general, rather than the specific, mechanisms involved in associative learning. Hence, we emphasize the following as primary features of learned behavior: pairing specificity, stimulus specificity, long-term retention (arbitrarily defined as lasting for at least 24 hr), a moderate degree of reversibility by subsequent experience (e.g. extinction), and demonstrations that nonassociative-learning processes cannot account for features a-c. Where appropriate, we also identified other interesting features of the learned behavior. It is apparent from the table that a major unresolved issue for most of the preparations is the extent to which the behavioral changes are exclusively associative. This is no less true for the vertebrate preparations than it is for the invertebrates. The clearest example of an exclusively associative behavioral change is the rabbit NMR. The learning-produced changes in the invertebrate preparations were all shown, to varying degrees, to be pairing specific. Yet a major unresolved issue is the degree to which apparent examples of associative-learning reflect complex interactions among basically nonassociative-learning processes. The core issue is really quite simple: Does the associative training procedure result in the acquisition of new or qualitatively different behavior; and is there a strict requirement for an associative relation? In addressing the adequacy of the neurophysiological analyses, the major issue is that of localization. Logically, there are two components to this.(ABSTRACT TRUNCATED AT 400
WORDS)

Cellular mechanisms of learning, *memory*, and information storage.
In Table 1, we summarize what is convincingly demonstrated to date for the major vertebrate and invertebrate *model* systems attempting to elucidate cellular mechanisms of associative learning. Two major concerns are the adequacy of the behavioral demonstrations and the completeness and extent of...
; *Aplysia*; Association Learning--Physiology--PH; Cats; Cerebellar Cortex--Physiology--PH; Cerebellum--Physiology--PH; Conditioning, Eyelid --Physiology--PH; Cyclic AMP--Pharmacology--PD; Geniculate Ganglion --Physiology--PH; Hippocampus--Physiology--PH;
Memory--Physiology--PH;
Motor Cortex--Physiology--PH; Photoreceptors--Physiology--PH; Rabbits; Reflex--Physiology--PH; Serotonin--Pharmacology--PD;
Synapses--Physiology
--PH

5/3,AB,KWIC/20 (Item 20 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05920453 85159814
Simulation of synaptic depression, posttetanic potentiation, and presynaptic *facilitation* of synaptic potentials from sensory neurons mediating gill-withdrawal reflex in *Aplysia*.
Gingrich KJ; Byrne JH
J Neurophysiol (UNITED STATES) Mar 1985, 53 (3) p652-69, ISSN 0022-3077 Journal Code: JC7
Contract/Grant No.: NS 19895, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The defensive gill-withdrawal reflex in *Aplysia* has proven to be an attractive system for analyzing the neural mechanisms underlying simple forms of learning such as habituation, sensitization, and classic conditioning. Previous studies have shown that habituation is associated with synaptic depression and sensitization with presynaptic *facilitation*

of transmitter release from sensory neurons mediating the reflex. The synaptic depression, in turn, is associated with a decrease in Ca2+ currents in the sensory neurons, whereas presynaptic *facilitation* with increased Ca2+ currents produced indirectly by a decrease in a novel serotonergic sensitive K+ current. The present work represents an initial quantitative examination of the extent to which these mechanisms account for each of these types of synaptic plasticity. To address these issues a lumped parameter mathematical *model* of the sensory neuron release process was constructed. Major components of this *model* include Ca2+-channel inactivation, Ca2+-mediated neurotransmitter release and mobilization, and readily releasable and upstream feeding pools of neurotransmitter. In the *model*, release of neurotransmitter has a linear function of Ca2+ concentration and is not affected directly by residual Ca2+. The *model* not only simulates the data of synaptic depression and recovery from depression, but also qualitatively predicts other features of neurotransmitter release that it was not designed to fit. These include features of synaptic depression with high and low levels of transmitter release, posttetanic potentiation, a steep relationship between action potential duration and transmitter release, enhanced release produced by broadening the sensory neuron action potential (presynaptic *facilitation*), and dramatic synaptic depression with two closely spaced tetraethylammonium (TEA) spikes. The *model* cannot account fully for synaptic depression with empirically observed somatic Ca2+-current kinetics. Rather a large component of synaptic depression is due to reduction to the pools of releasable neurotransmitter (depletion). In the *model* when spike durations are greater than 15-20 ms, spike broadening produces little *facilitation*. However, when spike durations are more physiological, spike broadening leads to enhanced transmitter release.

Simulation of synaptic depression, posttetanic potentiation, and presynaptic *facilitation* of synaptic potentials from sensory neurons mediating gill-withdrawal reflex in *Aplysia*.

The defensive gill-withdrawal reflex in *Aplysia* has proven to be an attractive system for analyzing the neural mechanisms underlying simple forms of learning such as habituation, sensitization, and classic conditioning. Previous studies have shown that habituation is associated with synaptic depression and sensitization with presynaptic *facilitation* of transmitter release from sensory neurons mediating the reflex. The synaptic depression, in turn, is associated with a decrease in Ca2+ currents in the sensory neurons, whereas presynaptic *facilitation* with increased Ca2+ currents produced indirectly by a decrease in a novel serotonergic sensitive K+ current. The present work represents an initial quantitative examination of the extent to which these mechanisms account for each of these types of synaptic plasticity. To address these issues a lumped parameter mathematical *model* of the sensory neuron release process was constructed. Major components of this *model* include Ca2+-channel inactivation, Ca2+-mediated neurotransmitter release and mobilization, and readily releasable and upstream feeding pools of neurotransmitter. In the *model*, release of neurotransmitter has a linear function of Ca2+ concentration and is not affected directly by residual Ca2+. The *model* not only simulates the data of synaptic depression and recovery from depression, but also qualitatively predicts other features of neurotransmitter release that it was not...

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; *Aplysia*; Models, Neurological; Neurons, Afferent--Physiology--PH; Synaptic Transmission

5/3,AB,KWIC/21 (Item 21 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05888820 89330482

Bistability and control for ATP synthase and adenylate cyclase is obtained by the removal of substrate inhibition.

Schiffmann Y
Department of Applied Mathematics & Theoretical Physics, University of Cambridge, United Kingdom.

Mol Cell Biochem (NETHERLANDS) Mar 16 1989, 86 (1) p19-40, ISSN 0300-8177 Journal Code: NGU
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

The thesis of this article is that the raison d'etre of the electron transfer chain and the receptor system is to remove 'substrate inhibition' of the enzymes ATP synthase and adenylate cyclase respectively. Activation by energization or hormone is analogous and presents the features of ideal control system; bistability, hysteresis, sensitivity and amplification, and rapid transitions between resting and active states. In the first part of the article, the simplest nontrivial *model* conforming with the experimental results is put forward. After the system is described, nonlinear and linear models are developed. An important aspect captured by the *model* is that the enzyme is structurally asymmetric corresponding to the assumption of regulatory site(s) distinct from catalytic site(s). The structural distinction between a regulatory site and a catalytic site entails different binding and specificity properties of the two types of sites with respect to the nucleotides. In the second part, the experimental evidence for the theory is discussed. It is shown that energization and hormone indeed reduce 'substrate inhibition' and that the properties of time lag and criticality predicted by the theory are indeed verified in experiment and are in turn explained by the theory. The theory can explain and correlate various hitherto unexplained experimental phenomena such as the irreversibility of ATP synthesis and the functional role of the ATP synthase asymmetry. The property of hysteresis predicted by the nonlinear *model*, is indicated by postillumination ATP synthesis, and preactivation of chloroplasts with reduced dithiols indeed display 'hysteresis loops'. In *Aplysia* *memory* for short term sensitization may reside in the hysteretic prolonged elevation of cAMP in sensory neurons.

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5/3,AB,KWIC/22 (Item 22 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05692605 90017529

Transformation of siphon responses during conditioning of *Aplysia* suggests a *model* of primitive stimulus-response association.

Walters ET
Department of Physiology and Cell Biology, University of Texas Medical School, Houston 77225.

Proc Natl Acad Sci U S A (UNITED STATES) Oct 1989, 86 (19) p7616-9, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: MH38726, MH, NIMH
Languages: ENGLISH
Document type: JOURNAL ARTICLE

A semi-intact preparation was used to study the effects of classical conditioning on the type of siphon response elicited by a conditioned stimulus to the mantle of *Aplysia*. Five pairings of the conditioned stimulus with an unconditioned stimulus to nerves from the tail transformed the constricting alpha response of the siphon into a conditioned flaring response resembling the unconditioned response to stimulation of the tail nerves. Although some pseudoconditioning occurred, an associative component was indicated by the significantly greater incidence of flaring responses after paired training than after unpaired presentations of the conditioned and unconditioned stimulus or the unconditioned stimulus alone. Previously described cellular plasticity in the underlying neural circuits suggests a testable *model* based on cell-wide rather than synapse-specific mechanisms, which can account for specific conditioned responses. In this *model*, effective stimulus-response associations are produced by a concatenation of stimulus-specific *facilitation* of sensory neurons (a mechanism for alpha conditioning) and response-specific *facilitation* of

motor neurons (a mechanism for pseudoconditioning).

Transformation of siphon responses during conditioning of *Aplysia* suggests a *model* of primitive stimulus-response association.
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Descriptors: *Aplysia*--Physiology--PH; *Conditioning, Classical; *Models, Neurological; *Models, Psychological; *Nervous System--Physiology
--PH

5/3,AB,KWIC/23 (Item 23 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05487397 89105834
Mathematical *model* of cellular mechanisms contributing to presynaptic *facilitation*.
Gingrich KJ; Baxter DA; Byrne JH
Department of Anesthesiology, Albany Medical College, NY 12208.
Brain Res Bull (UNITED STATES) Sep 1988, 21 (3) p513-20, ISSN 0361-9230 Journal Code: B5M
Contract/Grant No.: K02 MH00649, MH, NIMH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Presynaptic *facilitation* of transmitter release from sensory neurons is an important mechanism contributing to nonassociative and associative learning in *Aplysia*. In a previous modeling study (28,29), we concluded that enhancement of the postsynaptic potential (PSP) during presynaptic *facilitation* is mediated by at least two processes; spike broadening, which has been observed experimentally, and a process that we modeled as mobilization of transmitter. In an effort to gain insight into the relative contribution of these two mechanisms of presynaptic *facilitation*, we have extended our earlier *model* to include more detailed descriptions of: a) the kinetics of the Ca2+ channel, b) the diffusion of Ca2+ through the cytoplasm, c) the process of transmitter release, and d) the PSP. The present quantitative *model* provides an accurate description of the input-output relationship for synapses of sensory neurons, and predicts changes in the shape of postsynaptic potentials as a function of mobilization and spike broadening. The results confirm and extend previous experimental studies (33) and indicated that cellular analogs of sensitization (*facilitation* of nondecremented responses) is mediated primarily by spike broadening; whereas, analogs of dishabituation (*facilitation* of depressed responses) require mobilization.

Mathematical *model* of cellular mechanisms contributing to presynaptic *facilitation*.
Presynaptic *facilitation* of transmitter release from sensory neurons is an important mechanism contributing to nonassociative and associative learning in *Aplysia*. In a previous modeling study (28,29), we concluded that enhancement of the postsynaptic potential (PSP) during presynaptic *facilitation* is mediated by at least two processes; spike broadening, which has been observed experimentally, and a process that we modeled as mobilization of transmitter. In an effort to gain insight into the relative contribution of these two mechanisms of presynaptic *facilitation*, we have extended our earlier *model* to include more detailed descriptions of: a) the kinetics of the Ca2+ channel, b) the diffusion of Ca2+ through the cytoplasm, c) the process of transmitter release, and d) the PSP. The present quantitative *model* provides an accurate description of the input-output relationship for synapses of sensory neurons, and predicts changes in the shape of postsynaptic potentials as a function of mobilization and spike broadening. The results confirm and extend previous experimental studies (33) and indicated that cellular analogs of sensitization (*facilitation* of nondecremented responses) is mediated primarily by spike broadening; whereas, analogs of dishabituation (*facilitation* of depressed responses) require mobilization.
; *Aplysia*--Physiology--PH; Mathematics; Neuronal Plasticity

5/3,AB,KWIC/24 (Item 24 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05034182 87140233
Site-specific sensitization of defensive reflexes in *Aplysia*: a simple *model* of long-term hyperalgesia.
Walters ET
J Neurosci (UNITED STATES) Feb 1987, 7 (2) p400-7, ISSN 0270-6474 Journal Code: JDF
Contract/Grant No.: MH38726, MH, NIMH; NS00848, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Brief, noxious, electrical or mechanical stimulation of the skin of *Aplysia* produces enhancement of defensive reflexes triggered at the same site for at least a week after the noxious stimulation. This site-specific behavioral sensitization can be expressed as an increase in duration of the siphon-withdrawal reflex and as an increase in magnitude of the tail-withdrawal reflex. It is unlikely that peripheral factors play a predominant role in the long-term *memory*. First, long-term enhancement is blocked when the CNS is disconnected from the noxious stimulation site by nerve transection. Second, long-term enhancement is blocked by preventing neural activation at the noxious stimulation site, indicating that persistent physical damage alone is insufficient to cause the enhancement. A role for activity-dependent extrinsic modulation (ADEM) of mechanosensory neurons is suggested by similar site-specific enhancement produced when weak sensory activation is paired with general modulation elicited by strong stimulation of a distant site. Because this pairing represents a form of classical conditioning, site-specific sensitization and cutaneous classical conditioning appear to be closely related in this system. These findings suggest that site-specific sensitization reflects, at least in part, a central, long-term *memory* of injury. This form of *memory* may be phylogenetically widespread, and functionally similar to aspects of hyperalgesia. In addition, the close relationship between site-specific sensitization and cutaneous classical conditioning supports the hypothesis that some forms of classical conditioning evolved from mechanisms of sensitization.

Site-specific sensitization of defensive reflexes in *Aplysia*: a simple *model* of long-term hyperalgesia.
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Descriptors: *Aplysia*--Physiology--PH; *Conditioning, Classical --Physiology--PH; *Reflex--Physiology--PH; Denervation; Electric Stimulation; Hyperalgesia--Physiopathology--PP; *Memory*--Physiology--PH;
Physical Stimulation; Stereotyped Behavior; Tail--Innervation--IR

5/3,AB,KWIC/25 (Item 25 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

04928269 86226493
Identification of the neural pathway for reinforcement of feeding when *Aplysia* learn that food is inedible.
Schwarz M; Susswein AJ
J Neurosci (UNITED STATES) May 1986, 6 (5) p1528-36, ISSN 0270-6474
Journal Code: JDF

Languages: ENGLISH
Document type: JOURNAL ARTICLE
Bilateral sectioning of the esophageal nerves that innervate the gut of *Aplysia* was found to have profound effect on response decrement to inedible food: Time to criterion for cessation of feeding was elevated, no *memory* of the decrement was present 24 hr after training, and motor patterning during training was altered. The parametric features of response decrement to sustained lip stimulation were examined to determine their resemblance to parameters of response decrement to inedible food after esophageal nerve sectioning. Parameters of response decrement were similar, indicating that after esophageal nerve sectioning response decrement is likely to be the result of sustained lip stimulation. Bilateral nerve sectioning had no effect on decrement due to sustained lip stimulation. Unilateral lesions and lesions of either of the two major divisions of the esophageal nerves had no effect on learning that food was inedible. The data indicate that bilateral nerve sectioning eliminates all stimuli causing negative reinforcement of feeding due to failure to consume food. Based on the data in this and the previous paper, a *model* is presented suggesting sites of action and mechanisms for learning that foods are edible or inedible in *Aplysia*.

Identification of the neural pathway for reinforcement of feeding when *Aplysia* learn that food is inedible.
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Descriptors: *Aplysia*--Physiology--PH; *Feeding Behavior--Physiology--PH ; *Food; *Learning; *Reinforcement (Psychology); Denervation; Esophagus --Innervation--IR; Lip--Physiology--PH; *Memory*; Nervous System--Anatomy
and Histology--AH; Neural Pathways--Physiology--PH; Neuronal Plasticity; Physical Stimulation; Time Factors

5/3,AB,KWIC/26 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04557491 85113977
The pharmacology of molluscan neurons.
Rozsa KS
Prog Neurobiol (ENGLAND) 1984, 23 (1-2) p79-150, ISSN 0301-0082
Journal Code: Q3R
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW
It is commonly accepted that the basic physiological properties of the neurons as well as the nature of transmitter substances have remained relatively unchanged through evolution, while brain size and neuron number have greatly increased. Among invertebrates the molluscs, due to the large size of their neurons and lesser complexity of the neural networks controlling specific behavior, have proved to be especially useful for studying elementary properties of single neurons, network organization as well as various forms of learning and *memory*. The study of putative neurotransmitters has indicated that molluscs use the same low molecular-weight substances and peptides or their metabolites and cyclic nucleotides as transmitters and second messengers as the other species of various phyla. At the same time the receptors of neurotransmitters were found to have certain characteristic properties in the molluscs. The large molluscan neurons have permitted the isolation of individual identifiable nerve cells, and the subsequent analysis of quantities of the transmitters and their metabolic enzymes. These studies have demonstrated that single neurons frequently can contain more than one putative neurotransmitter. It can be expected that this *model* will contribute to an understanding of the role of multiple transmitters within a single neuron assuring the plasticity of the nervous system. The cellular mechanisms of plasticity have been demonstrated first in molluscan nervous systems. It was proved in identified *Aplysia* neurons that the same transmitter (ACh) can be released from an interneuron onto two or more follower neurons and can excite one and inhibit another or evoke a biphasic response on a third type of cell. The biphasic response of the molluscan neurons to neurotransmitters was the first demonstration of the plastic synaptic changes. The discovery of individual neurons with their groups of follower cells acting as chemical units has provided an insight into the organization of various behavioral acts. Study of the gastropod molluscs has also shown that the giant serotonergic cells can act as peripheral modulator neurons, as well as interneurons, and in this way they can affect their target organs at more than one level.The molluscan studies have provided more information on transmitter receptors as it was shown that molluscan neurons have at least six different 5HT receptors, three Ach receptors which can be separated pharmacologically. This type of study has led to the discovery of numerous new antagonists and poisons.(ABSTRACT TRUNCATED AT 400 WORDS)

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...; Central Nervous System--Metabolism--ME; Electrophysiology; Feeding Behavior--Physiology--PH; Ganglia--Physiology--PH; Heart--Physiology--PH; Histamine--Physiology--PH; Kidney--Physiology--PH;
Learning--Physiology--PH
; *Memory*--Physiology--PH; Neurons--Cytology--CY;
Neurons--Physiology--PH
; Neurotransmitters--Metabolism--ME; Neurotransmitters--Physiology--PH; Nucleotides--Physiology--PH; Peptides--Metabolism--ME; Receptors, Adrenergi
c--Metabolism--ME; Receptors...

5/3,AB,KWIC/27 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04540133 83215425
Presynaptic calcium diffusion and the time courses of transmitter release and synaptic *facilitation* at the squid giant synapse.
Zucker RS; Stockbridge N
J Neurosci (UNITED STATES) Jun 1983, 3 (6) p1263-9, ISSN 0270-6474
Journal Code: JDF
Contract/Grant No.: NS 15114, NS, NINDS; NS 11613, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
At the squid giant synapse, a presynaptic action potential is accompanied by an influx of calcium ions that continue to be detectable with arsenazo III microspectrophotometry for several seconds. Nevertheless, transmitter release occurs phasically, lasting only about 2 msec. If a second action potential follows within about 100 msec after the first, it releases more transmitter. In this paper, we present a mathematical *model* of intracellular calcium diffusion with binding to fixed cytoplasmic sites, active extrusion at the surface, and influx during an action potential, to predict the distribution of intracellular calcium following an action potential. With a square law relation between submembrane calcium and transmitter release, the *model* predicts the phasic release of transmitter and the magnitude and time course of synaptic *facilitation* following an action potential, as well as the relatively long persistence of free intracellular calcium.

Presynaptic calcium diffusion and the time courses of transmitter release and synaptic *facilitation* at the squid giant synapse.
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long persistence of free intracellular calcium.
; Action Potentials; *Aplysia*; Axons--Metabolism--ME; Axons--Physiology--PH; Diffusion; Neurotransmitters--Metabolism--ME; Squid; Synapses--Metabolism--ME; Time Factors

5/3,AB,KWIC/28 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04515267 81075273
Mathematical *model* of synaptic plasticity: III. Heterosynaptic changes.
Lara R; Tapia R; Cervantes F; Moreno A; Trujillo H
Neurol Res (ENGLAND) 1980, 2 (2) p137-52, ISSN 0161-6412
Journal Code: NY9
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A mathematical *model*, using differential equations, of heterosynaptic plasticity is proposed. The *model* is based on physiological studies of invertebrates in which nonspecific conditioning, such as sensitization and heterosynaptic inhibition, starts to be elucidated and behavioral studies of classical and instrumental conditioning, which we postulate to have the same mechanisms as those found in nonspecific conditioning. The *model* permits us to simulate the following heterosynaptic changes: sensitization, heterosynaptic inhibition, classical and instrumental conditioning--includi ng short- and long-term *memory* --extinction and recuperation--spontaneously and by stimulation.

Mathematical *model* of synaptic plasticity: III. Heterosynaptic changes.
A mathematical *model*, using differential equations, of heterosynaptic plasticity is proposed. The *model* is based on physiological studies of invertebrates in which nonspecific conditioning, such as sensitization and heterosynaptic inhibition, starts to be elucidated and behavioral studies of classical and instrumental conditioning, which we postulate to have the same mechanisms as those found in nonspecific conditioning. The *model* permits us to simulate the following heterosynaptic changes: sensitization, heterosynaptic inhibition, classical and instrumental conditioning--includi ng short- and long-term *memory* --extinction and recuperation--spontaneously and by stimulation.
; *Aplysia*; Computers; Models, Neurological; Neural Inhibition; Synaptic Transmission

5/3,AB,KWIC/29 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03984945 84023605
Behavioral changes in aging *Aplysia*: a *model* system for studying the cellular basis of age-impaired learning, *memory*, and arousal.
Bailey CH; Castellucci VF; Koester J; Chen M
Behav Neural Biol (UNITED STATES) May 1983, 38 (1) p70-81, ISSN
0163-1047 Journal Code: 9KH
Contract/Grant No.: MH35729-01, MH, NIMH; NS14385, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The marine mollusc *Aplysia* californica was used to examine the effects of age on simple forms of learning, *memory*, and arousal. We have found that aging impairs the long-term retention of habituation and prevents the acquisition of sensitization in the siphon withdrawal reflex. In addition, aging reduces arousal as evident in the heart rate component of the response to food stimuli. Our results are similar to the age-dependent alterations in the capacity for behavioral plasticity that have been reported in a variety of vertebrates, including man. These similarities suggest that the mechanisms underlying the effects of age on behavior and its modification may share common features across phyla and therefore might be studied to advantage in *Aplysia* whose central nervous system is especially accessible to cell biological approaches.
Behavioral changes in aging *Aplysia*: a *model* system for studying the cellular basis of age-impaired learning, *memory*, and arousal.
The marine mollusc *Aplysia* californica was used to examine the effects of age on simple forms of learning, *memory*, and arousal. We have found that aging impairs the long-term retention of habituation and prevents the acquisition of sensitization in the siphon withdrawal reflex...

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Descriptors: Aging; **Aplysia*--Physiology--PH; *Arousal--Physiology--PH; *Learning--Physiology--PH; Habituation (Psychophysiology)--Physiology--PH; Heart Rate; *Memory*--Physiology--PH; Reflex

5/3,AB,KWIC/30 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03122974 80008009
Synaptic *facilitation* in *Aplysia* explored by random presynaptic stimulation.
Kroeker JP
J Gen Physiol (UNITED STATES) Jun 1979, 73 (6) p747-63, ISSN 0022-1295 Journal Code: I8N
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The identified interneuron L10 in the abdominal ganglion of *Aplysia* was stimulated to fire action potentials in a random sequence while the early inhibitory potential of its follower cell L2 was recorded. Application of Wiener nonlinear analysis to these data yielded a predictive *model* of the facilitating postsynaptic potential. The *model* shows that *facilitation* changes both the time-course and the magnitude of the early synaptic potential. The facilitated response has a longer duration than the unfacilitated response. Its magnitude is exponentially decreasing with increasing interstimulus interval between test and conditioning stimuli. *Facilitation* is abolished at short interstimulus intervals. The hypothesis that the magnitude only of transmitter release is increased cannot explain these results. The observed *facilitation* may be due to characteristics of pre- and postsynaptic morphology.
Synaptic *facilitation* in *Aplysia* explored by random presynaptic stimulation.
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Descriptors: *Aplysia*--Physiology--PH; *Ganglia--Physiology--PH

5/3,AB,KWIC/31 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03078617 76207626
Frequency *facilitation* and post-tetanic potentiation of a unitary synaptic potential in *Aplysia* californica are limited by different processes.
Schlapfer WT; Tremblay JP; Woodson PB; Barondes SH
Brain Res (NETHERLANDS) Jun 4 1976, 109 (1) p1-20, ISSN 0006-8993
Journal Code: B5L
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Post-tetanic potentiation (PTP) of the monosynaptic and unitary excitatory postsynaptic potential (EPSP) recorded in cell R15 of the abdominal ganglion of *Aplysia* californica was observed after repetitive stimulation of the right visceropleural connective. PTP at this synapse developed after a few pulses (about 20) and after trains of low frequency stimulation (1/2 sec) under normal physiological conditions of media and temperature. No phase of post-tetanic depression was observed. Evidence is presented that the PTP is due to an increase in transmitter release. The amplitude of the PTP was a function of the frequency and number of stimuli in the preceding train. The PTP was observed to decay, with a single exponential time course, to the size of an isolated EPSP. The rate constant of PTP decay depended upon both the frequency and number of stimuli in the preceding train. The magnitude of the various types of synaptic plasticities seen at this junction, i.e., synaptic depression, frequency *facilitation* and PTP, correlated with the size of an isolated EPSP as well as with each other. Based on the analysis of the data in terms of a flow *model* of transmitter release, it is concluded that: (a) during a

train of repetitive stimulation the net rate of transmitter supply into the immediately available pool (net transmitter mobilization) increases, the efficiency of the release mechanism (fractional release) increases, and the pool of immediately available transmitter depletes; (b) upon the cessation of the train, as the peak amplitude of PTP is approached, the increased but diminishing rate of net transmitter mobilization refills the available pool to its equilibrium size, while the fractional release is still elevated; (c) during the PTP period after the peak potentiation, the elevated fractional release slowly decays with a single exponential time course; (d) the size of the facilitated EPSPs during the train is limited by the net rate of transmitter supply, although the efficiency of release is also increased; while the size of the EPSPs during the falling phase of the PTP period is determined solely by an increased efficiency of the release mechanism; and (e) the rising phase of the PTP observed in the period shortly after termination of the train is produced by the refilling of the depleted pool of available transmitter in the presence of an elevated release efficiency.

Frequency *facilitation* and post-tetanic potentiation of a unitary synaptic potential in *Aplysia* californica are limited by different processes.

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Facilitation at neuromuscular junctions: contribution to habituation and dishabituation of the *Aplysia* gill withdrawal reflex.

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The gill withdrawal reflex of *Aplysia* has been used as a *model* for studying the neuronal mechanisms of habituation, a behavioral plasticity. We have assessed the contribution of neuromuscular *facilitation*, an elementary synaptic plasticity, during habituation of the reflex by recording gill muscle potentials, which we show are caused by excitatory junctional potentials. These potentials show systematic frequency-dependent changes in amplitude. The gill withdrawal evoked by central motor neuron firing during each habituation trial is determined by *facilitation* of the excitatory junctional potentials during the trial and the facilitated state of the initial excitatory junctional potential in a trial, determined by neuron activity prior to the trial. The neuromuscular junctions, therefore, act like a frequency-dependent amplifier of central motor activity. They are fully responsive to the dynamic changes of motor neuron firing that occurs during habituation and especially after dishabituation.

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